A Review of Literature on the Estimation of Alkaloids for the Year 1904.

By *W. A. Puckner.*

Two interesting contributions, discussing in a general way the methods of estimating alkaloids in drugs were published in 1904. One, by E. Beuttner[1] discussed a series of publications by Panchaud on the valuation of Drugs, the work having been done at the request of the Swiss Pharmacopoeia Commission, the other, by G. Fromme[2] reviews both Panchaud's and Beuttner's conclusions.

Panchaud's publications were devoted to a general discussion of the Keller method which he considers far superior to all others, and to its application, with proposed modifications, to the various alkaloidal drugs.

Beuttner agrees with Panchaud that the water added in the Keller method, to cause the drug to separate in masses, may be the cause of an error because alkaloids are not entirely insoluble in water or in water containing an alkali, but that this error is not large unless an unnecessarily large volume is added.

While Panchaud recommends that, in the examination of tinctures and fluidextracts, they be distributed over sand and dried, Beuttner does not approve of this because the product is hygroscopic and can therefore not be transferred quantitatively and because emulsions are sometimes formed. Instead he suggests to concentrate the tincture or fluidextract in a flask to a small volume and then to add very little water, the required volume of ether or ether-chloroform

[1] Schweizerische Wochenschrift, 1904, 42, 57.
[2] Geschäfts-Bericht, 1904, Caesar & Loretz.

mixture and then 1—2 Gm. ammonia water. By reducing the ammonia water added, the total aqueous fluid need not be more than 6—12 Gm., which is less than in the "sand method."

Beuttner agrees with Panchaud that ammonium hydroxide should be given the preference over sodium hydroxide in liberating the alkaloid, but notes that usually the amount used is excessive and says that 1—2 Gm. of ten percent ammonia water is quite sufficient.

Fromme discusses the work of Panchaud and Beuttner in considerable detail and concludes:

While a very fine powder is more easily and more quickly extracted, most drug are readily exhausted when not so finely powdered and, since it is not an easy matter to reduce certain drugs to so fine a powder it should be directed only when there is real need for it as in golden seal.

Air dried drug is to be preferred over that dried at 100 degrees C. and if desired, moisture may be determined in a separate portion.

Whether ether, chloroform or a mixture of the two is to be preferred depends on the nature of the alkaloid to be extracted. If the alkaloid is sufficiently soluble in ether then this should be used since it is less liable to form emulsions; in ipecac it must be used since it rejects an inert alkaloid.

Generally ammonium hydroxide is to be used to set free the alkaloid. Exceptions are drugs containing volatile alkaloids where the ammonia dissolved by the ethereal solvent can not be wholly expelled by heat and where sodium hydroxide is to be preferred. As a result of many trials he also uses it in cinchona assays.

With few exceptions one-half to one hour's digestion of the drug with the alkali and solvent is sufficient if the mixture is shaken frequently.

Usually no difficulty is experienced in decanting a clear aliquot portion of the solvent and hence the addition of water is superfluous; when the alkaloid to be estimated is soluble in water then it of course is objectionable. Paper filters are not permissible when an aliquot portion is to be taken: they may cause an error as high as 10 percent. Cotton may be used: if the ethereal fluid is not perfectly clear it may be shaken with 1 Cc. water and this drawn off.

In a general way Panchaud's "simplified method" which requires

no separatory funnel and no volumetric alkali, is to be commended. The method directs the drug to be shaken with the volatile solvent, then the required alkali added and the mixture shaken for a specified time. After standing a rest for a time as much as possible of the clear supernatant fluid is poured into a conical flask, weighed, a portion of the solvent and with it all the ammonia, is distilled off and in the remaining liquid, adding hematoxylin, alcohol and, toward the end, water, the alkaloid is determined by titration with tenth-normal hydrochloric acid.

Fromme questions the advantage of doing away with the volumetric alkali: often an excess of alkali is added accidentally and then a residual titration must be resorted to. He also suggests the substitution of tenth-normal volumetric ammonium hydroxide and explains the desirability of combining a gravimetric determination with the titration as a check on the identity of the alkaloid.

Aconite. While G. Fromme[3] found that considerable care must be exercised to completely remove the volatile alkaline ammonium derivatives before titrating the alkaloidal residue obtained in the examination of aconite root, Beuttner[4] has been unable to demonstrate the presence of such volatile bases. The method which he proposes and which assumes the absence of these volatile bases, gave results which agreed well with those obtained by the Keller method were ether was used as a solvent and the alkaloidal residue either weighed or titrated.

For tincture of aconite root he directs: 60 Gm. are evaporated in a beaker, with frequent stirring, to 10 Gm. and poured into a tared vial. To the beaker one drop ammonia water is added and it is then rinsed with ether and this added to the contents of the vial until it contains 60 Gm. ether. Then 1 Gm. ammonia water is added, the vial stoppered and shaken frequently during 15 minutes. After standing at rest for 15 minutes, 50 Gm. are decanted through a pledget of cotton into a 200 Cc. flask. The ether is evaporated (distilled) until about 10 Gm. remain, then 5 Cc. absolute alcohol, 30 Cc. ether and three drops hematoxylin solution added and tenth-normal hydrochloric acid run in until the watery layer is reddish-

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[3] Caesar & Loretz Geschäfts-Bericht, 1903.
[4] Schweizer. Wochenschrift, 1904, 42, 74.

brown, then 30 Cc. water added and the titration continued until, after shaking, the watery layer is lemon-yellow.

The Mydriatic Drugs. It is now well known that the mydriatic drugs quite generally contain volatile bases[5] and that the varying results obtained when assaying the mydriatic drugs, particularly henbane, by different methods were due to the retention of varying proportions of volatile bases in the residue finally titrated.

Beuttner[6] finds that when ether is used in the valuation of belladonna leaves, and precautions are taken to completely expell the volatile bases that an almost pure alkaloid is isolated as shown by weighing and subsequently titrating the alkaloidal residue. He directs to macerate 15 Gm. powdered belladonna leaves with 95 Gm. dilute alcohol for 24 hours; 50 Gm. are then to be filtered off and reduced in a tared dish or beaker to 12 Gm. When cool, sufficient water to make 15.2 Gm. is added and the mixture then filtered. Of this filtrate 12 Gm. are shaken with 60 Gm. ether, and 1 Gm. ammonia water during 15 minutes and then put aside for 15 minutes. Of the ethereal layer 50 Gm., considered to represent 5 Gm. drug, are poured through cotton into a dry flask and the ether driven off. The residue is dissolved in 5 Cc. ether and brought to dryness three times and then titrated.

Fromme has compared Beuttner's method with his own, a modification of Keller's method in which ether is used as solvent and where care is taken to expell all volatile bases, and finds that both yield good results and that in each the weight of the residue agrees with that calculated from a titration.

W. K. Forstberg[8] compares several methods proposed for the valuation of belladonna leaves and prefers the following: 20 Gm. very finely powdered drug, dried at 100° C., are moistened with 20 Cc. 20% soda solution and brought to dryness on a water bath. The dry material is transferred to a vial, 90 Gm. ether and 30 Gm. chloroform are added, and after standing one-half hour 10 Cc. sodium hydroxide solution, 20%, are added, the mixture shaken frequently during 2 hours, then 20 Cc.

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[5] Merck's Bericht, 1900, p. 11; Fromme, Caesar & Loretz Geschäfts-Bericht, 1901, p. 62; H. Thoms, Apotheker-Ztg. 18, p. 389 (C. 1903, 2, p. 215).

[6] Schweiz. Wochenschrift, 32, p. 101.

[8] Pharm. Post 38, p. 2 (Chem. Centrbl. 1905, 1, p. 409).

water added, and after standing at rest during one hour 60 Gm. poured off. One-fourth of the ethereal fluid is distilled off, the remainder transferred to a separator, the flask rinsed with three portions of ether, 5 Cc. each, and shaken with 20 Cc. normal (? W. A. P.) hydrochloric acid, then 5 drops of eosin solution are added and the excess of acid determined with hundreth-normal alkali.

E. Leger[9] uses magnesium hydroxide for the liberation of alkaloids in drugs because ammonia water is liable to contain pyridin which will contaminate the extracted alkaloids and can only be removed if the alkaloids are dried thoroughly at 100° C. If ammonia water is to be used it should be freed from pyridine by shaking with chloroform. For belladonna leaves he directs to mix the dry powder with magnesium oxide and water. After 10 hours washed ether, i. e. ether free from alcohol and saturated with water, is added and the mixture shaken frequently during 12 hours. An aliquot part of the ether solution is then taken, the ether distilled off, the residue dissolved in neutral ether and titrated.

Cinchona. While some progress has been made in the valuation of cinchona in that the difficulty of completely extracting the alkaloids by ether or ether chloroform in presence of alkali has been more fully recognized little has been accomplished toward the elaboration of a ready means of estimating the proportion of quinine in the total alkaloids.

G. Fromme[10] has studied Panchaud's method and compares it with the method proposed by himself. Panchaud directs to add to 3 Gm. very finely powdered drug 30 Gm. chloroform and 90 Gm. ether then after 10 minutes 3 Gm. 10% ammonia water and shakes frequently for one hour. After standing at rest during five minutes, 100 Gm. of the clear ether-chloroform solution are poured off and reduced to 10 Gm. by destillation. To the residue 30 Cc. ether, 10 Cc. alcohol, hematoxylin solution and 10 Cc. water are added and then titrated with tenth-normal hydrochloric acid, further 30 Cc. water being added toward the end of the titration.

Fromme's method directs to heat 2.5 Gm. fine or coarse powder, 2 Cc. 25% hydrochloric acid and 20 Cc. water, contained in a 200 Cc. flask for 10 minutes on a water bath, and when cold to add 50

[9] J. Pharm. Chim. (6) 19, p. 923 (Chem. Centrlblt. 1904, 1, p. 1461.
[10] Geschäfts-Bericht v. Caesar & Loretz, 1904, p. 18.

Gm. ether, 25 Gm. chloroform and after shaking vigorously for a moment to render alkaline with 5 Cc. 15% sodium hydroxide solution and then to shake the mixture continuously and vigorously during 10 minutes. Then 3 Gm. powdered tragacanth are added, the mixture shaken thoroughly and at once 60 Gm. of the clear ether-chloroform solution filtered off. This is reduced to one-half its bulk. After adding 20 Gm. ether, the alkaloids are extracted by shaking successively with 10 Cc. tenth-normal hydrochloric acid, 10 and 10 Cc. water. To demonstrate that all alkaloid has been removed the ethereal liquid is extracted with 5 cc. tenth-normal acid and one drop of this tested with Mayer's solution. If free from alkaloid this extraction is rejected, else it is added to the first extraction and the ether extracted with several portions of water and this also added to the first extraction. The excess of acid is then determined and from the difference the weight of alkaloid calculated.

A bark by Panchaud's method gave 4.499, 4.460, 4.864, 4.864, 5.10, 4.250%. By Fromme's method 6.584, 6.773 and 6.448% was indicated. And when the finished titrations were rendered distinctly acid, extracted with ether to remove resinous matter, then made alkaline with ammonia and extracted with ether-chloroform, the solvent distilled off, the residue when dried and weighed indicated 6.565, 6.5000 and 6.460%. From a series of comparative estimations then made it appears, that the ether-chloroform, although more is used than in the original Keller method, does not extract the alkaloids quantitatively and that the direct method of titration as proposed by Panchaud does not determine the true alkalinity of the alkaloidal solution.

E. Beuttner[11] adapts Panchaud's method to the preparations of cinchona. For the valuation of the fluidextract he directs to place 3 Gm. fluidextract, 4 Gm. alcohol, 6 Gm. water and 5 Gm. sand in a 200 Cc. flask and to heat the mixture on a water bath until the contents are reduced to 12 Gm. When cooled, 90 Gm. ether 30 Gm. chloroform and 1 Gm. ammonia water are added and the mixture shaken during 15 minutes. After then standing at rest during 15 minutes, 100 Gm. are decanted through cotton and brought to dryness. The residue is dissolved in 10 Cc. absolute alcohol, 10 Cc. water, 30 Cc. ether, 3 drops hematoxylin solution added and then

[11] Schweiz. Wochenschrift 42, p. 74.

titrated with tenthnormal hydrochloric acid. A drug which by Panchaud's method assayed 6.8%, yielded a fluidextract which by this method assayed 6.74%. In the light of Fromme's experiments this agreement may be because the exhaustion of the drug in the assay and in the manufacture of the fluidextract was equally incomplete.

E. Leger[12] reports results obtained with four different methods. In 1. the drug is shaken for 12 hours with a mixture of alcohol, ether and ammonia water, in 2. chloroform and ammonia water, with macaration for 4 hours is directed; in 3. the drug is treated with magnesium oxide, solution potassium hydroxide and water, after two hours transferred to a continuous extractor and exhausted with chloroform; in 4. six Gm. drug are macerated for 1 hour with 6 Cc. ammonia water, 24 Cc. alcohol and then 120 Cc. ether added and macerated with frequent shaking during 6 hours. Then 120 Cc., taken to represent 4.8 Gm. drug, are filtered off and distilled to complete dryness. The residue is dissolved in 12 Cc. of a solution containing 1 Cc. strong hydrochloric acid in 14 Cc. and filtered to remove resinous material. Of the filtrate, 10 Cc. are rendered alkaline and extracted with chloroform. After distilling off the chloroform, the residue is dried at 100° C. and weighed. The results were: 1) 7.44%, 2) 7.96%, 3) 7.4% and 4) 8.36%.

B. M. Overton[13] also published some comparative estimations which illustrate the difficulty of exhausting cinchona.

J. Warin[14] discusses the valuation of cinchona by precipitating the alkaloids as cinchotannates from a hydrochloric acid extraction of the drug. He finds that, no matter whether acetic acid or sodium acetate be used, the precipitation is incomplete, and that on washing the precipitate a part dissolves, whether the water contains acetic acid or not. Comparative results may be obtained by closely following details. He prefers first to estimate the alkaloids and then, if needed, the tannin, in the solution from which the alkaloid was removed.

While, as stated before, methods for the separation of quinine from other cinchona alkaloids are still far from satisfactory, yet some advance is made. E. Leger[15] has studied the details of Andre's

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[12] J. Pharm. Chim. (6) 19, p. 479 Chem. Centralbl. 1904, 2, p. 161.

[13] Merck's report, 1904, 13, 353.

[14] J. Pharm. Chim. (6) 19, p. 233; Chem. Centrlbl. 1904, 1, p. 1110.

[15] J. Pharm. Chim. (6) 19, pp. 281, 434; Chem. Centrlbl. 1904, 1, pp. 1180, 1624).

bromine-ammonia test for quinine and finds that it can be used for quantitative estimations only if close attention be paid to all details, and that the directions contained in the Italian and Swiss pharmacopoeias are faulty.

E. Leger[16] has also studied the composition of the precipitated tartrates obtained from a mixture of cinchona alkaloids. He elaborates a method which, while complicated, appears to yield correct results.

B. H. Paul[17] and D. Howard[18] discuss the B. P. ether test for cinchonine and cinchonidine in quinine sulphate. While Paul upholds the ether test, Howard prefers the test of the French Codex.

N. Matolcsy[19] gives the following modification of the ether test: Measure 50 Cc. of the solution of the quinine salt to be tested into a 100 Cc. cylinder, render alkaline with sodium hydroxide solution, add 20 Gm. powdered sodium chloride and 20.2 Cc. absolute ether. Shake 5 to 10 minutes, pipette 10 Cc. to a tared dish, evaporate, dry at 100° C. and weigh. The salt so reduces the solubility of ether in water that 50 Cc. of water dissolve only 0.2 Cc.

Coca. For the valuation of coca leaves E. Leger[1] employs a a method practically identical with that given for belladonna leaves. He notes that the alkaloids can not be determined gravimetrically because one of the coca alkaloids, namely hygrine, is volatile.

Beuttner[2] studied Panchaud's method for the valuation of coca leaves and found it unsatisfactory. He says that aparently the leaves contain a basic non-alkaloidal body which can not be completely expelled from the alkaloidal residue even though the latter is repeatedly dissolved in ether and again brought to dryness. In a method for the examination of the fluid extract, ether is used to extract the alkaloids and the alkaloids are finally dried at 100° C. and weighed.

Goldenseal. Fromme found when, in the assay of goldenseal, an excess of ammonia water is added to the acid solution containing the hydrastine and this then shaken with ether, that from the

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16 J. Pharm. Chim. (6) 19, p. 427; Chem. Centrlbl. 1904, 1, 1624.

17 Chemist & Druggist 1902, 2, 65, 428, 506.

18 Chemist & Druggist, 1904, 2, pp. 65, 475, 556.

19 Pharm. Post 37, p. 177; Chem. Centrlbl. 1904, 1, p. 1299.

1 J. Pharm. Chim. (6), 19, p. 1460.

2 Schw. Wochenschft. 42, p. 105.

ethereal solution, at first perfectly clear, crystals of hydrastine will soon separate out. This has been fully confirmed and has no doubt often been the cause of lack of concordance in the results of hydrastine estimations. Fromme[3] finds that 20 parts ether for 1 part drug is sufficient to retain the alkaloid in solution and directs: 6 Gm. very finely powdered goldenseal, 100 Gm. ether, 20 Gm. petroleum ether and 5 Gm. 10% ammonia water are shaken frequently and vigorously for one-half hour, and, after the drug has settled, 100 Gm. decanted through cotton into a separator. From this the alkaloid is extracted with 30, 20, 10, 10 Cc. one-half percent hydrochloric acid. The acid solution is then made alkaline with ammonia water and extracted with 30, 20, 10, 10 Cc. ether. The ether is distilled off and the residue dried to constant weight.

Ipecac. It having been shown that when ether is used to extract the ipecac alkaloids the psychotrine is not taken up, this solvent has replaced the chloroform or ether-chloroform formerly used. On the other hand the separate estimation of emetine and cephaeline, as proposed by Paul and Cownley has not been generally adopted or found successful. Two methods have appeared during the year: One, by E. Beuttner[4] uses ether as a solvent, thus rejecting the inert alkaloid; the other, by E. Leger[5] uses a mixture of ether and chloroform and therefore estimates the "total" alkaloids.

Nux Vomica. E. Leger[6] gives two methods for the estimation of alkaloids in nux vomica. E. Beuttner[7] discussed the valuation of nux vomica preparations. Both recommend methods based on that of Keller and estimate the total alkaloids, i. e. do not distinguish between strychnine and brucine.

Opium. Lyman F. Kebler[8] presents co-operative work on opium assaying undertaken at the instance of the Association of Official Agricultural Chemists and in which participated: Blome, Dohme, Doolittle, Havenhill, Kebler, Lyons, Mallinckrodt Chemical Works, Puckner, Ruddiman and Smith. The specimen of powdered opium

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3 Geschäfts-Bericht v. Caesar & Loretz, 1904, 64.
4 Schwz. Wochenschft., 42, p. 89.
5 J. Pharm. Chim. (6), 19 p. 479; Chem. Centrbl. 1904, 2, p. 160.
6 J. Pharm. Chim. (6) 19, p. 479; Chem. Centrbl. 1904, 2, p. 160.
7 Schwz. Wochenschrft. 42, p. 77.
8 Proc. A. Ph. A., 52, p. 369.

sent out was assayed according to the method of the U. S. P. 1890, the lime method of the U. S. P. 1880 and the B. P., and the A. B. Stevens modification of the lime method. The morphine obtained by the first two methods was then tested (1) by determining the percent of loss when dried at 110 degrees, (2) by titrating with tenth-normal sulphuric acid, (3) by dissolving in a known excess of tenth-normal alkali and, after filtering from undissolved matter, determining the amount of acid in excess of that required to neutralize the added alkali, and (4) by determining its solubility in lime water. The results showing in a striking manner the unsatisfactory condition of morphiometry, are discouraging. While the chemists co-operating in this work, presumably, all have considerably experience in the testing of opium their results are widely discordant, showing a variation of more than five percent of the actual morphine present between the highest and lowest. By far the most concordant results were obtained by Stevens' method.

G. Fromme[9] reports regarding the nature of the impurities which are thrown down when, after adding ammonia water and ether, 24 hours are allowed for the separation of the morphine. In one case he found a lithium salt, usually it was calcium meconate. When following the short Helfenberger method and allowing only 10 minutes for the separation, then morphine was obtained which left no ash on ignition and when titrated required exactly the theoretica-volume of volumetric acid.

P. Schidrowitz[10] published a method for the estimation of morphine in opium which gives results agreeing with the methods used by dealers and manufacturers and which are said to be kept secret. The opium is moistened with water and after 15 minutes is triturated with more water and transferred to a flask and after one hour an aliquot part is filtered off. This is mixed with a solution of sodium salicylate, filtered and in an aliquot portion of this filtrate the morphine precipitated by ammonia water in presence of ether. Finally the morphine is estimated with volumetric acid, using methyl-orange as indicator in the titration of alkaloids; this would seem a step in the right direction, although Kippenberger[11] reports the contrary. Since this indicator is especially sensitive toward weak

[9] Geschäfts-Bericht v. Caesar & Loretz. 1904, 55.

[10] The Analyst 29, p. 144; Chem. Centrbl., 1904, 2, p. 160.

[11] Z. anal. Chem. 39, p. 201.

bases a sharp end-point should be obtained provided of course that its rather faint color is not obscured by the colored impurities of the morphine.

C. E. Caspari[12] has worked out a method of estimating codeine in opium which promises more correct results that those obtained by Van der Wielen's process, this being the only previously published method. A specimen of powdered Smyrna opium yielded 1.12% and 1.33% codeine, which is about the percent. reported in the opium specimens examined by Van der Wielen and shows the statements found in text-book to the effect that opium contains 0.2 to 0.6% codeine, to be wrong.

Pomegranate. Panchaud modified the method of the German Pharmacopoeia by substituting ammonia for sodium hydroxide, by omitting the addition of water before taking the aliquot portion, by substituting ether for the mixture of ether and chloroform and by titrating the alkaloids directly after a part of the ether has been distilled off. He directs to shake, vigorously and frequently, during one hour 12 Gm. powdered bark with 120 Gm. ether and 10 Cc. ammonia water. Then 100 Gm. (10 Gm. bark) of the clear ether solution are poured off, reduced to 25 Gm. by destillation and titrated. G. Fromme[13] approves of the substitution of ether for the chloroform-ether mixture and especially the omission of the water since the alkaloids are quite soluble in water. Experiments showed however that when the three-fourths of the ether is distilled off that not all the ammonia is expelled, while when the ether is all distilled off, much alkaloid was lost, the alkaloids of pomegranate being volatile. Fromme's experiments indicate that the drug contained some salt of ammonium or similar body which was estimated along with the alkaloid when sodium hydroxide was used to set free the alkaloid and the decanted ether solution titrated directly. If on the other hand the ether was partly distilled off, besides the ammonia also some alkaloid appeared to pass over. Provisionally he proposes: To 12 Gm. finely powdered drug, contained in a 200 Cc. vial, 120 Gm. ether are added and shaken frequently for 10 minutes. Then 10 Cc. 10% sodium hydroxide are added, the mixture shaken thoroughly and frequently during one hour and put aside 10 minutes.

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[12] Proc. A. Ph. A. 52, p. 386.

[13] Geschäfts-Bericht v. Caesar & Loretz, 1904, p. 27.

As much as possible of the clear ether solution is poured into a 200 Cc. Erlenmeyer flask, weighed, distilled until 25 Gm. remain, then 10 Gm. water, 5 Gm. alcohol and 10 drops hematoxylin solution added, then tenth-normal hydrochloric acid run in until the aqueous layer is reddish-brown, and well shaken. Next 30 Cc. water added and titrated with frequent shaking until the aqueous layer is lemon-yellow. 1 Cc. tenth-normal hydrochloric acid = 0.01475 Gm. alkaloid.

Tobacco. Several contributions treating of the estimation of nicotine in tobacco appeared during 1904. In part these estimations have had for their object the study of the relation between alkaloidal content and quality of tobacco. The correct estimation of nicotine has also become important because of the large use of tobacco extract as a constituent of sheep dips. Since nicotine is one of the so-called volatile alkaloids its separation from ammonia and other volatile bases is not readily accomplished and nicotine estimations are far from accurate.

J. Toth[14] defends his method against criticisms by Pontag[15].

R. Kissling[16] liberates the alkaloid with sodium hydroxide and then extracts it with ether in a continous extraction apparatus. To expell ammonia he distills the ether slowly, then adds to the residue a little sodium hydroxide, drives the nicotine over by steam and titrates the alkaline destillate with sulphuric acid, using luteol as indicator.

Waldbott[17] liberates nicotine in tobacco solutions or nicotine solutions containing ammonium salt by means of sodium bicarbonate and extracts the alkaloid with chloroform. Using copper sulphate as indicator, he adds an excess of acid and then titrates back with alkali until a faint cloud is produced. The error due to ammonia liberated by the sodium bicarbonate is ordinarily not more than 0.2%.

J. A. Emery[18] finds that tabacco extracts sold for use in sheep dips are often adulterated with pyridine. This is estimated as nicotine in the methods of analysis usually used where the alkaloid is

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14 Z. f. Unters. Nahr.-Genussm. 7, p. 151; Chem. Centrlbl. 1904, 1, p. 840.
15 Z. f. Unters. Nahr.-Genussm. 6, p. 673; Chem. Centrlbl. 1903, 2, p. 729.
16 Chem. Ztg. 28, p. 775; Chem. Centrlbl. 1904, 2, p. 860.
17 Pharm. Centrh. 1904, 45, p. 192; Proc. A. Ph. A. 52, p. 949.
18 J. Am. Chem. Soc. 26, p. 1113; Chem. Centrbl. 1904, 9, p. 1347.

distilled with steam. Emery bases an estimation of nicotine in presence of pyridine on the optical inactivity of pyridine, nicotine being strongly laevogyre. First the total volatile bases are isolated by steam destillation in the usual way and determined by titration with acid and methyl-orange as indicator. To estimate the nicotine in the finished titration, its polarisation is compared with that of a solution of pure nicotine of known strength. The pyridine is then calculated from the difference between the titration and the polarization results.